

Vaccine confidence, public understanding and probity: time for a shift in focus?

Ana Wheelock^{1,2} and Jonathan Ives³

¹Department of Surgery and Cancer, Imperial College London, London, UK.

²Business School, Kingston University, London, UK.

³Centre for Ethics in Medicine, Population Health Sciences, University of Bristol, UK.

Corresponding author

Dr Ana Wheelock

Address: Department of Surgery and Cancer
Imperial College London
South Kensington Campus
London SW7 2AZ, UK

Email: a.wheelock@imperial.ac.uk

Mobile: +44(0)7908373208

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Abstract

Lack of vaccine confidence can contribute to drops in vaccination coverage and subsequent outbreaks of diseases like measles and polio. Low trust in vaccines is attributed to a combination of factors, including lack of understanding, vaccine scares, flawed policies, social media, and mistrust of vaccine manufacturers, scientists and decision-makers. The Covid-19 crisis has laid bare societies' vulnerability to new pathogens and the critical role of vaccines (and their acceptability) in containing this and future pandemics. It has also put science at the forefront of the response, with several governments relying on academics to help shape policy and communicate with the public. Against this backdrop, protecting public trust in scientists and scientific output is arguably more important than ever. Yet, conflicts of interest (CoI) in biomedical research remain ubiquitous and harmful, and measures to curb them have had limited success. There is also evidence of bias in industry-sponsored vaccine studies and academics are voicing concerns about the risks of working in a CoI prevalent research area. Here, we set out to challenge established thinking with regard to vaccine confidence, by shifting the gaze from a deficit in public understanding towards probity in research relationships and suggesting an alternative and perhaps complementary strategy for addressing vaccine mistrust. We argue that a concerted effort needs to be made to revisit the norms that undergird contemporary vaccine research, coupled with a willingness of all stakeholders to reimagine those relationships with an emphasis on demonstrating trustworthiness and probity.

Introduction

Immunisation is lauded as one of the most cost-effective public health interventions and a key strategy to reduce the spread of antimicrobial resistance¹, and most recently, a critical approach to halt the Covid-19 pandemic. However, the success of this public health intervention not only depends upon how effective, accessible and safe it actually is, but also upon how it is perceived.

Vaccine confidence is a term frequently used to describe the belief that vaccines are protective, safe and part of a trustworthy medical system². In the past two decades, vaccine confidence has suffered a series of setbacks³, prompting the World Health Organization (WHO) to recognise it as one of the top ten threats to global health⁴. Low vaccine confidence is attributed to a combination of factors, including lack of understanding, vaccine scares, flawed policies, the spread of anti-vaccination messages via social media⁵ and mistrust of vaccine manufacturers and decision-makers⁶. This crisis of confidence has led to drops in vaccination coverage and subsequent outbreaks of diseases like measles and polio^{3,7}.

Unlike therapeutic treatments aimed at curing or alleviating existing conditions, vaccines are designed to prevent a potential disease, which makes them particularly vulnerable to omission bias – the preference for harm caused by omissions (e.g. not vaccinating) over equal or lesser harm caused by acts (e.g. vaccinating)⁸. Omission bias can be exacerbated if people have reservations about the trustworthiness of the vaccine development, approval and implementation processes, especially when children’s safety is at stake⁹.

Challenges to vaccine confidence are global, but they are most salient in high-income countries (HICs)^{10,11}, where vaccines and healthcare are more accessible, vaccine-preventable diseases are less prevalent and visible, and education levels higher. The impact of this trend is illustrated by the UK’s loss of its WHO ‘measles-free’ status¹² and France’s move to make eight additional vaccines mandatory to increase uptake¹³. In adults, inaction or active vaccine refusal are more common, also resulting in inadequate coverage^{14,15}.

The first global survey on attitudes toward science found that low confidence in vaccines is also associated with distrust of scientists¹¹. Our own analysis of this dataset revealed that only 33% of HICs participants trust ‘a lot’ that academic scientists seek to benefit the public and 22% trust ‘a lot’ that academics are honest about who funds their work¹⁶, suggesting low overall levels of trust in academic research. Lack of trust in scientists – particularly among those who distrust vaccines – adds a new dimension to the well-established literature on the links between vaccine uptake and trust in vaccines, government and vaccine manufacturers^{6,17}.

The Covid-19 crisis has laid bare societies' vulnerability to new pathogens and the critical role of vaccines (and their acceptability) in containing this and future epidemics. It has also put science at the forefront of the response, with several governments relying on academics to help shape policy and communicate with the public. However, being at the frontline of a fast-moving epidemic could act as a double-edged sword. On one hand it can provide much needed expertise in support of governments' response and highlight the value of science, but on the other hand, if 'science-led' policy decisions are opaque, flawed or inappropriately executed, or if experts' independence is questioned, it can hurt the credibility of academics and their work – and concerns have been voiced by some in the academy that the rhetoric of 'science led' policy is disingenuous¹⁸.

Against this backdrop, protecting public trust in scientists and scientific output is arguably more important than ever – and this not only requires us to take seriously and engage with peoples' concerns, but also to demonstrate trustworthiness. In the case of vaccines, however, most interventional efforts to improve vaccine confidence continue to disregard the potential legitimacy of people's concerns and focus on educating, incentivising or coercing them, with suboptimal results; the few randomised trials that have tested these approaches have shown they are minimally effective in increasing uptake and vaccine mandates have often backfired when confidence is low². Notably, the behaviour of academics and vaccine manufacturers, as well as the nature and appropriateness of their relationships, remain largely under-researched and unchallenged.

In this paper, we set out to challenge established thinking with regard to vaccine confidence, by shifting the gaze from a deficit in public understanding towards probity in research relationships and proposing an alternative and perhaps complementary strategy for addressing vaccine mistrust. Our intention is not to argue this will resolve all problems or should replace other strategies, but to point towards an approach that may be fruitful. In doing so, we also posit that a perceived information/understanding deficit is unlikely to work without tackling head on the question of trust and probity.

Is a lack of trust in vaccine academics and their research reasonable?

Science studies scholars have long theorised about the ways in which publics understand and accept science, and what happens when they do not. Of particular relevance here is Wynne's argument that people cannot be expected to trust science if the integrity of the institutions that underpin it is compromised:

“One of the general dimensions along which people experience science, and along which they can have understandings of it which scientists typically do not recognise, is that of its

institutional structures of accountability, pluralism or hegemony, patronage, ownership and control. This logically affects the public's readiness to assimilate the contents of science"¹⁹.

Accepting this, we propose that lack of confidence in vaccine science needs to be understood within the context of an economic and political system that consistently favours the economically advantaged, which has led to widespread dissatisfaction with the performance of democracies and low trust in the *elites*²⁰⁻²². A prominent beneficiary of this system is the pharmaceutical industry, which in recent years has become the most profitable industry sector²³. Their success, however, has been underpinned by unethical behaviour and aggressive tactics that have tarnished their reputation^{24,25}.

Integral to the pharmaceutical industry's business model are collaborations with academia, which have led to the discovery of life-saving medical technologies and treatments – and which we have relied on to develop some Covid-19 vaccines²⁶. This model began to take shape during the Reagan administration in the 80s, when the US Congress passed a series of laws – notably the Bayh-Dole act²⁷ – to facilitate the translation of publicly funded discoveries into successful products, several of which would end up in industry's pockets²⁸. Different versions of this model have been adopted elsewhere²⁹. Angell points out that before this pro-business shift took place, there were two clear and separate paths for scientists; they could either “choose to live a comfortable but not luxurious life in academia, hoping to do exciting cutting-edge research or they could “sell out” to industry and do less important but more remunerative work”²⁴. Since then, the interests of industry, researchers and academic institutions have become more entwined and, arguably, conflicting; and we suggest this is likely to be an important factor in public trust in vaccines.

We understand conflicts of interest as “a set of conditions in which professional judgement concerning a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)”³⁰. Although conflicts of interest do not always lead to unethical behaviour, it can compromise the integrity of academics and introduce biases that lead to harm. The insidiousness of such bias is well documented; even small gifts such as stationary or coffee can influence the behaviour of those at the receiving end, sometimes unwittingly³¹.

A comprehensive report by the U.S. Institute of Medicine provided a sobering overview of how varied and ubiquitous financial conflicts of interest (for brevity, henceforth ‘CoI’) was in medical research³² (see Box 1).

Box 1. Key findings from the Institute of Medicine report on conflicts of interest

- Researchers fail to disclose payments from industry.
- Unfavourable results from industry-sponsored clinical trials led by academic researchers are not published.
- Academic researchers co-author manuscripts ghost-written by industry employees that report results from studies they were not involved in.
- Researchers who develop clinical guidelines cover up their financial ties with industry.

Although there is little research on the impact of industry funding on the integrity of vaccine academics and their work, there is some indication that CoI are also prevalent and bias-inducing in this area of research. For example, 85% of vaccine clinical trials are sponsored by vaccine manufacturers and non-industry trials are over four times more likely to report negative or mixed findings than industry-sponsored trials³³. Beutels also found that an industry-sponsored economic evaluation of vaccination scored worse in methodological appropriateness than a comparable non-industry evaluation³⁴.

The facts are, however, mostly irrelevant, because in matters of trust, perception is all; and it is certainly a reasonable assumption that perceived CoI in vaccine studies will impact on the trusted status of vaccine academics and trust in the science itself. An illustrative example of how the involvement of vaccine manufacturers in clinical trials and policymaking can not only sow mistrust in the science behind a particular vaccine, but also affect entire immunisation schedules, is the aftermath of the introduction of mandatory human papilloma virus (HPV) vaccination in the U.S.

Although the adoption of school mandates was hindered by multiple factors, including the newness of the vaccine and the sexual nature of HPV, Congrove and colleagues found that the involvement of the vaccine manufacturer, Merck, was particularly damaging³⁵. Dismay over Merck's intervention in the policy process, including the provision of funds to an organisation of female legislators that introduced many of the bills to mandate HPV vaccination, also put in doubt the government's true motivation "to force pharmaceutical products on minors"³⁵. This was quickly picked up by a prominent anti-vaccine organisation, who accused Merck of deceiving the public and concealing important safety information³⁶. Strikingly, a principal investigator of HPV vaccine trials for Merck and GlaxoSmithKline agreed that "It seemed very odd to be mandating something for which 95 percent of infections never amount to anything"³⁷. Further, a recent review showed that design problems in the HPV vaccine trials, most of which were led by academics but sponsored by industry, made it difficult to evaluate the extent to which the vaccine prevented cervical cancer³⁸. These more recent developments are likely to increase public concern about the efficacy and safety of the HPV vaccine.

This controversy has proven contagious, not only resulting in persistent low uptake of the HPV vaccine³⁹, but also decreased uptake of other vaccines³⁵. One response to these concerns – and a response that is typical of current models to increase vaccine uptake – is not to engage with the issues that lead to lack of trust, but to assume that lack of vaccine confidence flows from a deficit in understanding and/or that people need to be pushed into it (with varying degrees of force). These models assume the problem is lack of knowledge and/or gullible acceptance of *alternative facts*, and as such, are unlikely to be effective if the problem is in fact lack of trust because (1) the people and institutions attempting to remedy the supposed problem are the very people and institutions that are not trusted and (2) where there is no trust, attempts to nudge or coerce are likely to be strenuously resisted. Yearly (in a systematisation of empirical environmental studies) cautioned that the costs of ignoring people’s concerns are high and often long-lasting⁴⁰.

The introduction of the HPV vaccine in the U.S. is one of several examples of how distrust in a vaccine, and the causes of that distrust, can have wide and perduring consequences – including the extrapolation to other vaccines, with potentially catastrophic consequences for public health^{41–42}, such as the recent drop in MMR vaccination in the Philippines (88% to 55%), largely due to reported risks of a new dengue vaccine⁴³.

Partnerships between academia and vaccine manufacturers can not only affect the trustworthiness of vaccines and vaccine science, but can also be costly for individual researchers, regardless of their discipline. In a recent commentary, a group of academics describe the “hazards” experienced by vaccine researchers, including being ostracised by peers for challenging the status quo, being attacked by anti-vaccine groups and working in a CoI prevalent research area⁴⁴. This resonates with the experience of one of us (ID removed) and anecdotal evidence from colleagues working in vaccines, some of whom have reported feeling conflicted and stigmatised by peers for receiving industry funding.

While CoI and problems of bias in vaccine research are not new, their visibility has been significantly increased by accessible online information outlets and social networks. “Collusion” between academics and vaccine manufacturers is a common grievance among members of the public or organisations who are concerned about or against vaccines⁴⁵. Although high-profile basic researchers are frequent targets of criticism, the integrity of social scientists can also be called into question, as illustrated in Box 2.

Despite the fact that vaccine actors are a clear source of concern about vaccines, and despite evidence of bias in industry-funded vaccine research that suggest some concern is reasonable, probity in academia-industry relationships and their impact on vaccine confidence have been largely absent from public health ethics debates. Instead, in line with much social sciences research, ethical inquiry has

centred on the behaviour of the public and the pros and cons of compulsory vaccination⁴⁶⁻⁴⁹, with a primary focus on changing wrong behaviour, as opposed to taking seriously and addressing the (at least *prima facie* legitimate and understandable) concerns that may lead to that behaviour.

The current coronavirus epidemic is a stark reminder of the extent to which public health relies on public trust⁵⁰. Yet, trust in public health interventions, in this case vaccines, is not formed in a

Box 2. Examples of opinions from members of the public about vaccine researchers

Twitter exchange in response to a comment from Peter Hotez, professor of paediatrics and molecular virology and microbiology

@PeterHotez

Wow, just wow: The evidence that #vaccines DO NOT & CANNOT cause #autism is detailed in my new book @amazon <https://amazon.com/Vaccines-Did-Not-Cause-Rachels-Autism/dp/1421426609>. I think it's an outrage that the @thehill published this unbridled @antivax @antiscience viewpoint. Awful. #VaccinesWork

@cgammicchia

So y ou [sic] are saying the [Department of Justice's] "expert" witness was wrong? They hid the information and covered it up! Just because it's in your pro-vax book doesn't mean it's correct. Plus you have a conflict of interest on this topic don't you? #vaccinehavecausedautism

@JakeLCrosby

Petey was on @GSK's vaccine policy advisory board when he led a pro-vaccine petition against "misinformation," also around the same time @GSK stole medical records of Dr. Wakefield's patients and gave them to @DeerBrian⁵²

Rapid response to an interview with Heidi Larson, professor of anthropology, risk and decision science

"It was interesting that Professor Heidi Larson expresses unease about those who take a questioning view of the vaccine industry and it's [sic] products. Many people, and I am one, have spent a professional lifetime reassuring parents that vaccines for children must be effective and safe, as the experts tell us that is so. Alarmingly, once one examines the evidence, or lack of it, that allows vaccine experts to be so confident, one discovers that the expected confirmatory evidence, for the safety and effectiveness of vaccines, is, very often, just not there... No doubt Professor Larson is aware of this, and those of us who realise that her Vaccine Confidence Project is partly funded by GSK can imagine the difficulties that conflicts of interest may cause in the amount of attention accorded to such information."⁵³

vacuum; it is inextricably linked to the trustworthiness of the institutions involved in their development, approval and implementation^{6,11,51}. It is, therefore, plausible that one of the reasons why containing vaccine *hesitancy* has proven so difficult is that little has been done to assuage legitimate concerns about the extent to which the motivations of experts, vaccine manufacturers and governments are aligned with the public interest.

O'Neill argues that trusting should not be "a matter of blind deference, but of placing – or refusing – trust with good judgement", which she refers to as "well-placed trust"⁵⁴. We believe that vaccines are generally beneficial, although we acknowledge that not all vaccines are created equal. We also hypothesise that the public's scepticism is a reasonable response to the problems that are visible to

them in the vaccine industry and at least some lack of confidence in vaccines may be a marker of well-placed mistrust.

Protecting the integrity of medical research: why is it so difficult?

To our knowledge, no specific measures aimed at protecting the integrity of vaccine researchers and their work have been proposed or implemented. However, in the 2000s, calls led by U.S. academics to improve transparency and regulate interactions between industry, professional medical associations, academic institutions and their researchers^{31,55-57} led to some positive results. For example, top academic medical centres implemented restrictions to gifts, food, honoraria, etc. originating from industry⁵⁸ and CoI began to be routinely declared in scientific journals. More recently, mandatory (U.S.) and voluntary (UK) publicly accessible registries have been created for declarations of interests between physicians (who may also work in academia) and the pharmaceutical industry⁵⁹. These improvements in transparency, whilst certainly positive, will do little to demonstrate trustworthiness where there is already a lack of trust but, rather, such declarations will provide circumstantial evidence of reasons to withhold trust.

Meanwhile, academia-industry collaborations continue to flourish, and researchers are still encouraged by universities and funders to develop links with industry^{60,61}, with some expressing concerns about their reputations and income if industry support is curbed⁵⁸. In some developed countries, the majority of panel members producing clinical practice guidelines have disclosed or undisclosed financial CoI⁶².

A similar trend can be observed in vaccine research⁶³, including Covid-19 vaccines⁶⁴. Current events aside, in the UK, for example, a government-backed vaccine network is bringing closer together industry, academia and relevant funding bodies to make targeted investments in vaccines and vaccine technology⁶⁵. Consequently, all aspects of most high impact, industry-sponsored clinical trials remain influenced by industry⁶⁶ and systematically produce more favourable efficacy findings and conclusions than research supported by other sources^{32,67}.

With plenty of evidence showing how the pharmaceutical industry has directly (e.g. biased research) or indirectly (e.g. mistrust) threatened public health^{68,69}, unregulated academia-industry relationships have the potential to inflict further damage during the Covid-19 pandemic and in years to come. This is because vigorous and urgent efforts to develop and produce Covid-19 treatments and vaccines, without appropriate and highly visible safeguards against conflicts of interest, could not only multiply and consolidate academia-industry relationships, but also fuel existing distrust in vaccine candidates. There is already some indication that the acceptability of Covid-19 vaccines may not be as high as we hoped. In recent polls, only 29% of people in the U.S. said they would definitely take the vaccine,

almost a third did not intend to vaccinate and were “pretty” certain that more information will not change their mind, and intention to vaccinate was linked to confidence in the research and development process⁷⁰. In the UK, over a third of people said they were unlikely to vaccinate and 48% felt concerned about safety⁷¹, and intention to refuse the vaccine was linked to beliefs and perceptions reflecting scepticism about scientific experts and government⁷².

An obvious reason why it has been so difficult to curtail CoI, is that there is no consensus among academic institutions about how to manage it⁷³. This is reflected in substantial variability in the contents and detail of institutional CoI policies (when one is available), and the way these policies are enforced⁷⁴. Notably, most CoI policies focus on disclosure rather than prevention.

This *ad hoc* and light touch approach to CoI, however, is likely to be influenced by a constellation of often interrelated factors. Given the lack of agreement about how to manage CoI and how normalised academia-industry partnerships are, it is perhaps unsurprising that many academics are still confused about what relationships constitute CoI and appear to have limited knowledge about why they may be morally contestable⁷⁵. Some argue that academic institutions have little incentive to regulate CoI, when the revenue generated by their partnerships with industry is so significant⁷⁶. Others believe that the focus on disclosure in the medical sciences may confer on physicians and researchers a kind of moral immunity that exempts them from their duty to deal with the issues raised by CoI⁷⁷. Thacker suggests that “many scientists are incapable of understanding and accepting that financial conflicts of interest corrupt science because they believe that scientists are objective and too well trained to be influenced by financial rewards, like all other human beings”⁷⁸.

Can the trustworthiness of vaccine science be improved?

CoI in biomedical research is a complex and pervasive problem. Whilst CoI are not only caused by academia’s relationships with industry, it is safe to say that these ties, in their current form, are a significant source of misconduct and mistrust^{45,67,68}. The relationships between academics and vaccine manufacturers are particularly problematic, not only because they threaten the integrity of academics and science, but critically because they erode public trust in vaccines and put public health at risk.

Certainly, overreliance on transparency (i.e. declaring CoI) as a strategy to improve trustworthiness has not been very effective. O’Neill suggests that one reason why public distrust has grown in an era of openness, is the realisation that transparency may not curtail intentional misinformation that weakens relations of trust, and that it is the risk of deception, not lack of transparency, that is the real enemy of trust⁵⁴. Transparency, albeit desirable, is not only insufficient to curb deception, but may also provide cover for it. Braillon rightly reminds us that transparency is just a tool, independence should be the goal⁷⁹. Angell²⁴ and, more recently, Moynihan and colleagues⁸⁰ have proposed

evidence-based and actionable pathways to disentangle academia from commercial interests, which warrant careful consideration (Box 3). Cutting ties between industry and other key actors, such as government authorities and regulatory agencies, may help to improve vaccine confidence, but the arguments for this will be complex and are outwith what we can achieve in this paper.

Given the lack of public debate about the need to improve the trustworthiness of vaccine research, or consensus about how to do it, there seems to be an obvious need to create a platform for public deliberation on the issue and to conduct high quality empirical research to explore trust and trustworthiness in vaccine development, and their impact on vaccine uptake. Understanding the problem holistically is an essential first step towards addressing it, and we suggest that one of the reasons that most contemporary attempts to address vaccine *hesitancy* have had limited effectiveness

Box 3. Possible strategies to cut ties between academia and industry

- Governments require that evidence used for healthcare decision making is independently produced and all public healthcare organisations and their advisers (who may also be academics) have no financial relationships with industry⁸⁰.
- Groups producing research syntheses provide reviewers with all available information on study methods and results and should be conducted without industry funding and by authors with no conflicts of interest⁸⁰.
- Academic groups engaged in educational activities for health professionals or the public, or advocacy influencing regulatory or policy decisions, sever financial ties with industry⁸⁰.
- Medical journals and their editors sever financial ties with industry⁸⁰.
- Research funding agencies and academic institutions modify metrics and incentives to reward academic collaboration with public agencies and civil society⁸⁰.
- An independent institute within a public research funding agency is created to administer clinical trials and act as an intermediary between academia and industry²⁴.

is the deep-rooted assumption that it is the behaviour of the public that needs changing, not the individual and collective behaviour of those charged with developing, approving, manufacturing, recommending and distributing vaccines. This is not to suggest that they systematically act wrongly – rather, that they do not take explicit and effective steps to demonstrate trustworthiness. A concerted effort, then, needs to be made to revisit the norms that undergird contemporary vaccine research, coupled with a willingness of all stakeholders to reimagine those relationships with an emphasis on demonstrating trustworthiness and probity.

This discussion has inexorably transformed into a call to address a deficit in the research agenda – and turn a critical gaze on the relationships between the actors that seem to have the most to gain from maintaining the status quo. The ethical imperative for doing so is, we hope, now clear. The status quo does not serve the public interest, and as long as it engenders mistrust, it threatens confidence in, and therefore the success of, one of our most effective public health measures.

We acknowledge that protecting the integrity of vaccine researchers and their work will take significant resolve and effort, and possibly a paradigm shift in how academia and industry relate to each other. Yet, in these turbulent times, where ‘unprecedented’ is a term routinely wielded, a serious questioning of science’s institutional structures of accountability, pluralism or hegemony, patronage, ownership and control may be possible.

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